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Factors influencing the early mortality in haematological malignancy patients with nosocomial Gram negative bacilli bacteraemia: a retrospective analysis of 154 cases

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ABSTRACT

Background: The aim of this study is to assess the factors influencing the early mortality (7-day after index blood culture) in haematological malignancy patients with Gram negative bacilli (GNB) bacteraemia.

Methods: Infection control committee records were reviewed to identify the cases between March 2006 and June 2011. Only one bacteraemic episode per patient was included in the study.

Results: A total of 154 patients with GNB bacteraemia were identified. The early mortality rate was 19.5% (30 out of 154). Blood cultures revealed Enterobacteriacea in 120 patients (*Escherichia coli*; 86, *Klebsiella* spp.; 28, *Enterobacter cloacea*; 6) and glucose non-fermenting GNB in 34 patients (*Pseudomonas aeruginosa*; 15, *Acinetobacter baumannii*; 11, *Stenotrophomonas maltophilia*; 7, *Burkholderia cepacia*; 1). Forty (33.3%) out of 120 Enterobacteriaceae were extended spectrum beta-lactamase (ESBL) producers and 18 (52.9%) out of 34 glucose non-fermenting GNB were multidrug resistant. Carbapenems were administered as first line therapy in 139 out of 154 patients. In univariate analysis Pitt's bacteraemia score, presence of aplastic anaemia, bacteraemia caused by glucose non-fermentating GNB, inappropriate empirical antibacterial treatment, presence of severe sepsis or septic shock, unable to achieve microbiological cure, and intensive care unit (ICU) acquired bacteraemia were associated with mortality. Multivariate analysis showed ICU acquired bacteraemia (OR, 12.55; 95% CI, 2.34–67.38, $p = 0.003$) as an independent factor associated with early mortality.

Conclusion: Haematological malignancy patients who require ICU care are at high risk for early mortality related to GNB bacteraemia. Based on the local findings pointing out high rate of multidrug resistance, carbapenems combined with colistin seems to be a reasonable approach as empirical treatment of these patients. However, increasing carbapenem resistance rate is of concern.

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Introduction

The increasing incidence of Gram-negative bacilli infections is of concern in patients with haematological malignancies or undergoing stem cell transplantation. Treatment is challenging due to the high rate of multidrug resistance.[1] High treatment costs and increased rate of mortality are well-known features of infections caused by multidrug resistant Gram negative bacilli (MDRGNB).[2] However, the relationship between antibacterial resistance and mortality is scarce. In two recent prospective observational studies, multidrug resistance (MDR) was reported to be associated with mortality in haematological malignancy patients with Gram-negative bacilli (GNB) bacteraemia, but the investigators were not able to show the impact of inappropriate empiric antibacterial therapy on mortality.[3,4] In our previous studies which evaluated the outcome of extended spectrum beta-lactamase (ESBL) producing *Escherichia coli* and MDR *Acinetobacter baumannii* bacteraemia in a group of patients with several immunocompromised conditions including haematological malignancies, we were not able to show the impact of MDR on mortality.[5–7] However heterogeneity of the underlying diseases, presence of co-infections with several opportunistic pathogens, and different epidemiological characteristics of the centres could have influenced these findings.

The aim of this study is to assess the outcome of nosocomial GNB bacteraemia in patients with haematological malignancy or undergoing stem cell transplantation and analyze the factors influencing mortality in our hospital.

Patients and methods

This study was conducted at Erciyes University Hospital, a 1300-bed tertiary care centre located in Kayseri, Turkey. The records of the infection control committee were retrospectively reviewed to identify the patients with monomicrobial nosocomial GNB bacteraemia between March 2006 and June 2011. Case patients were defined as those who were >16 years of age, had at least one blood culture positive for GNB and had clinical signs of systemic infection.[8] Only one bacteraemic episode per patient was included. This study was approved by the local ethics committee.

The following demographic data were extracted from patients' charts: age, gender, hospital length of stay prior to development of bacteraemia, and intensive care unit (ICU) stay, underlying haematological malignancy, neutrophil count at the day of blood culture, and receiving stem cell transplantation. The medical histories of the patients such as diabetes mellitus (DM), corticosteroid use, graft versus host disease, acute renal failure, chronic renal insufficiency requiring haemodialysis, hepatic insufficiency, coronary artery disease, congestive heart failure and chronic obstructive lung disease were also recorded. Severity of illness was calculated by the Pitt's bacteraemia score[9] and Charlson's weighted index of morbidity.[10] Nosocomial bacteraemia and the sources of bacteraemia were defined according to the criteria proposed by the Centers for Disease Control.[11] Bacteraemia that was detected after 72 h of ICU care in patients who did not have evidence of bacteraemia at admission was characterized as ICU acquired.[12] Severe sepsis was defined as sepsis with one or more signs of organ dysfunction. Septic shock due to GNB bacteraemia was characterized by positive blood culture with persistent arterial hypotension (defined as a systolic arterial pressure below 90 mmHg, mean arterial pressure <60 mmHg, or a reduction in systolic blood pressure of >40 mmHg from baseline) unexplained by other causes and in spite of adequate volume rehydration.[8]

The initial empirical antimicrobial therapy was considered to be "appropriate" if the initial antibiotics, which were administered within 24 h after collecting a blood sample for culture, included at least one antibiotic that was active in vitro (except ceftriaxone, cefotaxime and ceftazidime for ESBL producing Enterobacteriaceae) and when the dosage and route of administration were in accordance with current medical standards. Otherwise, the initial antimicrobial therapy was considered as "inappropriate".[5,7,13]

During the study period, GNB isolated from blood cultures were identified by automated systems and antimicrobial susceptibility and ESBL production were tested according to Clinical Laboratory Standards Institute (CLSI) recommendations.[14] Strains showing "intermediate" antimicrobial susceptibility profiles were considered to be resistant. Colistin susceptibility was determined by a disk diffusion test with 25 μg colistin (Oxoid, UK), according to the British Society for Antimicrobial Chemotherapy (BSAC) criteria. The isolates with a zone diameter of ≥14 mm were accepted as susceptible.[7] The strains of *Pseudomonas aeruginosa* and *A. baumannii* that were non-susceptible to ≥1 agent in ≥3 antimicrobial categories were defined as multidrug resistant (MDR) based on the recent consensus report.[15] *Stenotrophomonas maltophilia* that is intrinsically resistant to aminoglycosides and beta-lactam antibiotics including carbapenems is also defined as MDR. Microbiological cure was defined when the organism could not be isolated in repeat blood cultures during or after the course of therapy; failure was considered when cultures were persistently positive for the same organism or development of a superinfection with a microorganism other than initial GNB at least three days after treatment initiation.[16,17]

For statistical analysis, we divided the patients into two groups according to survival status 7-days after the first positive blood culture was obtained. All statistical analyses were performed with SPSS software for Windows (version 15.0; SPSS, Chicago, IL). Continuous variables were expressed as median values, first and third quartiles, categorical variables were expressed as the frequencies and percentages of the patients analyzed. Groups were compared with use of χ^2 and Fisher's exact tests for categorical variables, and the Mann–Whitney *U* test for continuous variables. In order to identify the independent risk factors for mortality, univariate and multivariate logistic regression analysis were used to control for the effects of confounding variables. Odds ratios (ORs) and their 95% confidential intervals (CIs) were calculated. All risk factors with potential association with mortality (whether they were statistically significant or not) and statistically significant variables in univariate analysis were included in the multivariate logistic model and backward stepwise selection was performed at a stringency level of $p < 0.10$ to determine the independent risk factors for 7-day mortality.[4,18] Measures of

the goodness-of-fit were obtained to assess the performance of the models. All *p*-values were two tailed, and $p < 0.05$ was considered statistically significant.

Results

A total of 154 patients with GNB bacteraemia were eligible for the study. Median age of the patients was 40.7 years (range; 16–76 years) and 86 were male. The most common underlying haematological malignancy was acute myelogenous leukaemia (AML). Twenty-five patients underwent allogenic stem cell transplantation (SCT) and 22 underwent autologous SCT. The demographic characteristics of the patients are shown in Table 1.

Of the total, 120 patients had bacteraemia caused by Enterobacteriaceae (*E. coli*; 86, *Klebsiella* spp.; 28, *Enterobacter cloacea*; 6) and glucose non-fermenting GNB were isolated in 34 patients (*P. aeruginosa*; 15, *A. baumannii*; 11, *S. maltophilia*; 7, *Burkholderia cepacia*; 1). Forty (33.3%) out of 120 Enterobacteriaceae were ESBL producers, and 18 (52.9%) out of 34 glucose non-fermenting GNB were MDR. All MDR strains of *P. aeruginosa* and *A. baumanni* were resistant to cefepime, ciprofloxacin, piperacillin/tazobactam, amikacin, and imipenem. Colistin was tested only against *A. baumannii* and all isolates were susceptible. Table 2 shows the antibacterial susceptibility profile of the causative GNB isolated from blood cultures.

All but two patients received empirical antibiotic therapy within an hour after the blood culture was performed. Carbapenems (imipenem, 105; meropenem, 32; doripenem, 2) were the treatment of choice in 139 patients (27 of whom died), five patients received piperacillin/tazobactam (one of whom died), two patients received cefoperazone/sulbactam (two of whom died), two patients received ciprofloxacin (none of them died), and two patients ceftriaxone (none of whom died). One patient who had an intrabdominal abscess received tigecycline and another patient suffering from catheter infection received teicoplanin as the empiric antibiotic therapy. Inappropriate empirical antibiotic therapy was more common in patients with poor outcome (43.3% vs 10.5%, $p < 0.001$). Since 10 out of 11 *A. baumannii* strains and 4 out of 15 *P. aeruginosa* strains were resistant to carbapenems, inappropriate antibacterial therapy was more common in patients with glucose non-fermenting GNB bacteraemia. Although none of the patients with *S. maltophilia* bacteraemia received empiric antibiotic therapy active against *S. maltophilia* only one patient died. Severe sepsis or septic shock was not detected in these patients and they did not receive ICU care. After the culture results became available trimethoprim/sulfamethoxazole was started in three patients and ciprofloxacin was the treatment choice in the other three patients with *S. maltophilia* bacteraemia.

We were able to evaluate microbiological cure in 66 out of 86 patients with *E. coli* bacteraemia, 27 out of 28 patients with *Klebsiella* spp. bacteraemia, 5 out of 6 patients with *Enterobacter cloacae* bacteraemia, 11 out of 15 patients with *P. aeruginosa* bacteraemia, 8 out of 11 patients with *A. baumannii* bacteraemia, and 7 out of 7 patients with *S. maltophilia* and 1 out of 1 *Burkholderia cepacia* bacteraemia. Microbiological cure was not achieved in 15 out of 125 evaluable bacteraemic patients (five with *E. coli* bacteraemia, three with *Klebsiella pneumoniae* bacteremeia, two with *E. cloacae* bacteremeia, four with *A. baumannii* bacteremia). Microbiological cure rate was significantly higher in surviving patients (81.5% vs 30.0%, $p < 0.001$) and being unable to achieve microbiological cure was associated with mortality (OR, 45.38; 95% CI, 10.34–199.14, $p < 0.001$) in the univariate analysis.

The mortality rates at 7-day, and at 14-day of bacteraemia were 19.5%, and 26%, respectively. Seven out of 154 patients died before culture results became available. Univariate analysis showed that high Pitt's bacteraemia score (OR, 1.79; 95% CI, 1.41–2.30, $p < 0.001$), presence of aplastic anaemia (OR, 4.16; 95% CI, 1.32–13.11, $p = 0.015$) as the underlying haematological disorder, bacteraemia caused by glucose non-fermenting GNB (OR, 3.09; 95% CI, 1.30–7.33, $p = 0.01$), inappropriate empirical antibacterial treatment (OR, 0.15; 95% CI, 0.06–0.39, $p < 0.001$), presence of severe sepsis (OR, 12.75; 95% CI, 5.03–32.35, $p < 0.001$) or septic shock (OR, 13.67; 95% CI, 1.37–136.48, $p = 0.026$), and ICU acquired bacteraemia (OR, 10.91; 95% CI, 3.02–39.38, $p < 0.001$) were associated with mortality. Duration of hospitalization (OR, 1.02; 95% CI, 0.99–1.04, $p = 0.17$), ESBL production in Enterobacteriaceae (OR, 0.73; 95% CI, 0.24–2.23, $p = 0.59$), MDR in glucose non-fermenting GNB bacteraemia (OR, 4.33; 95% CI, 0.91–20.6, $p = 0.07$) and severe neutropenia (neutrophil count < 100 cells/mm^3) (OR, 0.32; 95% CI, 0.02–4.51, $p = 0.40$) and neutropenia (neutrophil count < 500 cells/mm^3) (OR, 0.78; 95% CI, 0.02–25.4, $p = 0.89$) were not associated with mortality based on univariate analysis.

When multivariate analysis was performed to compare the relative contribution of risk factors associated with 7-day mortality, ICU acquired bacteraemia (OR, 12.55; 95% CI, 2.34–67.38, $p = 0.003$) was found to be independently associated early mortality. Of the 12 patients who were receiving ICU care during the onset of bacteraemia, MDR *A. baumannii* was isolated in three patients, MDR *P. aeruginosa* in two patients and ESBL producing *E. coli* was isolated in two patients. 11 out of 12 patients had severe sepsis and septic shock was diagnosed in one patient. While 7 of the patients with Enterobacteriaceae (*E. coli*; 4, *Klebsiella* spp.; 2, *E. cloacea*; 1) bacteraemia received appropriate antibiotic therapy, none of the patients with *A. baumannii* or *P. aeruginosa* bacteraemia received appropriate antibacterial therapy.

Discussion

Patients with haematological malignancies or receiving stem cell transplantation are highly vulnerable to serious infectious. Defining the causes of the attributable mortality is difficult in this group of patients. Several studies used 14 or 30-day mortality as the main outcome measure in haematological malignancy patients with GNB. However, this a very long time to detect the relationship between mortality and bacteremia, because patients with haematological malignancies have several cofounders for mortality particularly in a follow up period of 14 or 30 days.[3,4,19,20] So, we decided to use 7-day survival as the main outcome measure in this study. In this retrospective observational study the early mortality rate (7-days after index blood culture) was 19.5% among

Table 1 – Baseline demographic and clinical characteristics of the haematological malignancy patients with Gram negative bacilli bacteraemia.

Characteristics	Total $n = 154$	Non-survived $n = 30$ (%)	Survived $n = 124$ (%)	p value[a]
Age, median (range), years	40.7 (16–76)	47.5 (16–76)	40.0 (16–76)	0.31
Gender				0.76
Male	86 (55.8)	18 (60.0)	68 (54.8)	
Female	68 (44.2)	12 (40.0)	56 (45.2)	
Haematological diagnosis				0.02
Leukaemias	92 (59.7)	16 (53.3)	76 (61.3)	
Acute mylogenous leukaemia	63 (40.9)	13 (43.3)	50 (40.3)	
Acute lymphocytic leukaemia	26 (16.9)	3 (10.0)	23 (18.5)	
Chronic lymphocytic leukaemia	3 (1.9)	0	3 (2.4)	
Lymphoma	30 (19.5)	3 (10.0)	27 (21.8)	
Hodgkin lymphoma	13 (8.4)	2 (6.7)	11 (8.9)	
Non-Hodgkin lymphoma	17 (11.0)	1 (3.3)	16 (12.9)	
Multiple myeloma	17 (11.0)	4 (13.3)	13 (10.5)	
Aplastic anaemia	15 (9.7)	7 (23.3)	8 (6.5)	
Hematopoietic stem cell transplantation	47 (30.5)	5 (16.7)	42 (33.9)	0.1
Allogenic	25 (16.2)	5 (16.2)	20 (16.1)	
Autologous	22 (14.3)	0 (0.0)	22 (17.7)	
Comorbid diseases	15 (6.7)	5 (16.6)	10 (8.0)	0.17
Acute renal failure	10 (15.4)	4 (1.9)	6 (4.8)	
Graft versus host disease	3 (1.9)	0 (0.0)	3 (2.4)	
Diabetes mellitus	1 (0.6)	1 (3.3)	0	
Goodpasture syndrome	1 (0.6)	0 (0.0)	1 (0.8)	
Source of bacteremia				0.13
Primary bacteremia	111(72.1)	23 (76.7)	88 (71.0)	
Catheter related	27 (17.5)	2 (6.7)	25 (20.2)	
Other	16 (10.3)	5 (16.6)	11 (8.8)	
Pneumonia	5 (3.2)	4 (13.3)	1 (0.8)	
Urinary tract infection	6 (3.9)	1 (3.3)	5 (4.0)	
Abscess	5	0 (0.0)	5 (4.0)	
Duration from admission to bacteremia median (days) (range)	22.7 (1–92)	17.0 (1–92)	24.0 (1–55)	0.03
Corticosteroid use	16 (10.4)	5 (16.7)	11 (8.9)	0.31
Neutrophil counts				0.29
<100 cells/mm^3	123(79.9)	27 (90.0)	96 (77.4)	
100–500 cells/mm^3	13 (8.4)	1 (3.3)	12 (9.7)	
>500 cells/mm^3	18 (11.7)	2 (6.7)	16 (12.9)	
Pitt's bacteremia score, median (range)	1.27 (0–8)	2.5 (0–8)	0 (0–6)	<0.001
Charlson comorbidity index, median (range)	2.17 (0–6)	2.0 (0–4)	2.0 (0–6)	0.3
Severe sepsis	44 (28.6)	22 (73.3)	22 (17.7)	<0.001
Septic shock	4 (2.6)	3 (10.0)	1 (0.8)	0.024
Enterobacteriaceae	120 (77.9)	18 (60.0)	102 (82.3)	0.017
Escherichia coli	86	10	76	
Klebsiella pneumoniae	25	5	20	
Klebsiella spp.	3	0	3	
Enterobacter cloacea	6	3	3	
Glucose non-fermenting Gram negative bacilli	34 (22.1)	12 (40.0)	22 (17.7)	
Pseudomonas aeruginosa	15	3	12	
Acinetobacter baumannii	11	8	3	
Stenotrophomonas maltophilia	7	1	6	
Burkholderia cepacia	1	0	1	
Multidrug resistant non-fermenter Gram negative bacilli (n:34)	18 (52.9)	9 (75.0)	9 (40.9)	0.12
ESBL producing Enterobacteriaceae (n:120)	40 (33.3)	5 (27.8)	35 (34.3)	0.78
Intensive care unit acquired bacteraemia	12 (7.8)	8 (26.7)	4 (3.2)	<0.001
Inappropriate empiric antibiotic treatment	26 (16.9)	13 (43.3)	13 (10.5)	<0.001

ESBL, extended spectrum beta-lactamase.
Values are expressed as n (%) or median (25th and 75th percentiles).
[a] p Value for χ^2, Fisher's exact, and Mann–Whitney U test, were applicable.

Table 2 – Antibacterial susceptibility rates of the causative Gram negative bacilli isolated from blood cultures.

Microorganisms	IMP, %	SAM, %	TZP, %	CTX, %	CAZ, %	CFP, %	CIP, %	AN, %	NN, %	SXT, %
Escherichia coli (*n* = 86)	100	46.2	78.3	65.1	NA	NA	25.0	93.5	92.8	23.8
Klebsiella spp. (*n* = 28)	100	40.7	75.0	71.4	NA	NA	75.0	95.8	92.3	41.2
Pseudomonas aeruginosa (*n* = 15)	73.3	NA	86.7	NA	86.6	85.7	86.6	92.8	100	NA
Acinetobacter baumannii (*n* = 11)	9.1	20	18.2	0	0	0	9.1	22.2	85.7	11.1
Stenotrophomonas maltophilia (*n* = 7)	NA	NA	NA	NA	42.8	NA	85.7	NA	NA	100
Enterobacter cloacae (*n* = 6)	100	16.6	50.0	83.3	NA	NA	50.0	100	NA	16.6
Burkholderia cepacia (*n* = 1)	100	NA	NA	NA	100	NA	0	NA	NA	100

IMP, imipenem; SAM, ampicillin/sulbactam; TZP, piperacillin/tazobactam; CTX, cefotaxime; CAZ, ceftazidime; CFP, cefepime; CIP, ciprofloxacin; AN, amikacin; NN, netilmicin; SXT, trimethoprim/sulfamethoxazole; NA, not available.

haematological malignancy patients with GNB bacteraemia. The early mortality rate was found to be 18% in 51 cancer patients with MDRGNB bacteraemia which was not statistically different when compared to 312 patients with non-MDRGNB bacteraemia.[4] Based on the findings of the same study group, early mortality and overall mortality (30-days after the index blood culture) were similar in cancer patients with ESBL producing *E. coli* and non-ESBL producing *E. coli* bacteraemia.[19] Although inappropriate antimicrobial therapy was significantly more common in patients with poor outcome, we were not able to show significance of this finding in multivariate analysis. This is concordant with the recent studies evaluating the outcome of bacteraemia in patients with haematological malignancies.[4,19–21] However, not being able to adjust for differences between treatment groups receiving appropriate or inappropriate antibacterial therapy using multivariate techniques commonly used may have been the reason for this finding.[13]

Our findings showed ICU acquired bacteraemia as the only significant factor associated with mortality in the multivariate analysis. The prognosis of patients with haematological malignancies who are admitted to the ICU is generally poor and culture proven infection was reported to be related with poor outcome.[22,23] A recent study showed that GNB bacteraemia approximately doubled the risk of death in ICU patients.[12] Carbapenems should be the first choice in an endemic area of ESBL producing Enterobacteriaceae and addition of colistin in the empirical regimen can improve the outcome in the setting of MDR *A. baumannii* and *P. aeruginosa*. Although using carbapenems as first line therapy in the treatment of febrile neutropenic patients seems to be a reasonable approach when ESBL producing Enterobacteriaceae is common, the potential of triggering infections caused by carbapenem resistant glucose non-fermenting GNB is of concern. In a retrospective analysis of antimicrobial resistance in our intensive care units carbapenem resistance in *A. baumannii* doubled at the end of ten years.[24] De-escalation of carbapenems is an important strategy after blood culture results become available to avoid unnecessary use of broad spectrum antibiotics.

Aside from the statistical analysis the percentage of ESBL producing Enterobacteriaceae as high as 33.3% was significant. Fluoroquinolones have been widely used in our hospital in patients undergoing stem cell transplantation and receiving high dose chemotherapy for AML. Exposure to fluoroquinolone was reported to be associated with ESBL production in *E. coli* and *K. pneumoniae* as well as carbapenem resistance in *A. baumannii*.[25–27] Previous studies from our hospital and several hospitals around the country showed a high rate of cefepime resistance or ESBL production in *E. coli* and *K. pneumoniae*.[21,28–30] Such consequences led carbapenems to become first line therapy particularly in the treatment of febrile neutropenia in our hospital. However, the heavy use of carbapenems resulted in the emergence of a high rate of carbapenem resistant *A. baumannii* and *S. maltophilia* bacteraemia. When we checked the medical records of these patients we witnessed the use of carbapenems in the treatment of febrile neutropenia for several episodes. Due to the retrospective nature of study we could not test the clonality of isolates, but the patients were hospitalized at different time periods which excluded cross-transmission between patients. Although we did not experience any carbapenem resistance in Enterobacteriaceae, the first isolate of carbapenem resistant *E. coli* from Turkey was reported from a hospital with heavy use of carbapenems in treatment of ESBL producing *E. coli* bacteraemia.[31] A previous study from our hospital showed that piperacillin/tazobactam resistance was 44.7% in *E. coli*, 34.4% in *K. pneumoniae*, and 27.7% in *P. aeruginosa* isolated from febrile neutropenic patients.[28] After discontinuing piperacillin/tazobactam as first line therapy particularly in febrile neutropenic patients with long duration of hospitalization, currently the susceptibility to piperacillin/tazobactam is between 75 and 86.7% (Table 2). A recent post hoc analysis showed the efficacy of piperacillin/tazobactam in the treatment of ESBL producing *E. coli*.[32] Piperacillin/tazobactam monotherapy or in combination with amikacin seems to be a reasonable alternative for treating febrile neutropenia in our hospital to reduce carbapenem use particularly in patients with stable clinical condition. Such kind of policy evaluations could help all centres to avoid heavy carbapenem usage. Some institutions have some concerns about the use of piperacillin/tazobactam in the treatment of febrile neutropenia due to cross-reaction of the antibiotic with serum galactomanan antigenemia which is an important marker for early diagnosis of invasive aspergillosis. There are conflicting results about this interaction even studies from the same country in the same time interval.[33,34] However, there are at least two recent studies that showed no interaction between piperacillin/tazobactam and galactomannan antigen when original brand is used.[35,36]

Despite the efforts to implement infection control programmes MDRGNB infections seem to be an important problem for healthcare settings. Colistin is an alternative for the treatment of MDR *P. aeruginosa* and *A. baumannii* infections.

Clinical cure was achieved in 20 out of 26 haematological malignancy patients with MDR *P. aeruginosa* infections of whom 69% had bacteraemia.[37] Tigecycline has been considered as an alternative for MDR *A. baumannii* infections based on in vitro high susceptibility rates. Previously, we reported favourable outcome of carbapenem resistant *A. baumannii* wound infection in an AML patient treated with tigecyline.[17] However the serum concentration of tigecycline is low at standard dosing which warrants special consideration when using tigecycline in the treatment of bloodstream infections.[38]

Our study has some limitations. This a retrospective study from a single centre analysing heterogenous groups of GNB bacteraemia which do not share the same epidemiological and clinical characteristics. In addition, the types of haematological malignancies or stem cell transplantation were different which makes it difficult to generalize the findings for all patient groups. Additionally, using the infection control committee records to identify the cases could have missed the patients with bacteraemia at admission.

As a conclusion, the findings of this study did not prove the role of inappropriate empirical antimicrobial therapy in early mortality among patients with haematological malignancy or undergoing SCT. However, it is apparent that the initial empiric therapy in most cases (139 out of 154) included carbapenems and then, of course, it would have been difficult to single out inappropriate therapy as a risk factor, since carbapenems were appropriate treatment for most cases. ICU acquired bacteraemia was the only statistically significant risk factor for mortality. Special attention should be paid for the initial antibiotic therapy of haematological malignancy patients receiving ICU care or with severe sepsis with multiorgan failure. Since new antimicrobial regimens for MDRGNB is far away, institutional policies including the judicious use of antibacterials based on the local surveillance data and implementing infection control measures to avoid the spread of resistant microorganisms are essential.

Conflict of interest

All authors declare to have no conflict of interest.

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